DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

The Role of the National Institute of Allergy and Infectious Diseases in Research to Address the COVID-19 Pandemic

Testimony before the

United States Senate Committee on Health, Education, Labor, and Pensions

Hearing Titled:

Next Steps: The Road Ahead for the COVID-19 Response

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November 4, 2021

Madam Chair, Ranking Member Burr, and Members of the Committee:

Thank you for the opportunity to discuss the role of the National Institute of Allergy and Infectious Diseases (NIAID) in the research response to coronavirus disease 2019 (COVID-19) and its etiologic agent, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Within the Department of Health and Human Services (HHS) and the National Institutes of Health (NIH), NIAID is responsible for conducting and supporting basic and clinical research on emerging and re-emerging infectious diseases, including COVID-19. As the Director of NIAID and the Chief Medical Advisor to the President, I am pleased to discuss NIAID's research addressing this pandemic.

COVID-19 is a once-in-a-lifetime global infectious disease pandemic requiring an unprecedented public-private research effort. NIAID plays a central and important role in the public health response to COVID-19. In this regard, NIAID has capitalized on decades of investment in fundamental basic research, including groundbreaking structure-based vaccine design at the NIAID Vaccine Research Center (VRC); engaged domestic and international research infrastructure; and leveraged highly productive partnerships with industry and longstanding relationships with community partners.

NIAID utilized its existing domestic and international clinical trials infrastructure, originally established to conduct clinical research on HIV and influenza, and worked with partners in the public and private sectors to establish the COVID-19 Prevention Network (CoVPN). The CoVPN clinical trials network has supported multiple COVID-19 vaccine candidates to progress in record time from concept to authorization for emergency use by the U.S. Food and Drug Administration (FDA). NIAID also initiated clinical trials with creative and adaptive designs, allowing the evaluation of multiple new and existing therapeutics for use against COVID-19. Several of these trials provided evidence of safety and efficacy of COVID-19 therapeutics and helped support authorization by the FDA.

These successes have helped slow the progression of the pandemic in the United States, though challenges remain such as vaccine hesitancy and extending the durability and breadth of protection provided by COVID-19 vaccination. Currently, more than 69 percent

FDA-approved

group that periodically reviews data from the ongoing trials to ensure the safety of study volunteers and to determine whether efficacy has been achieved. The CoVPN has enrolled more than 41,000

COVID-19 four months or more after the second dose was maintained at greater than 90 percent. In addition, in observational studies in "real-world" conditions in broader segments of the population, mRNA-based vaccines continue to display high levels of effectiveness.

On June 26, 2021, FDA updated the EUAs for the Moderna and Pfizer COVID-19 vaccines to include information on the potential risks of myocarditis and pericarditis, particularly following the second dose. According to CDC, reports of myocarditis and pericarditis following vaccination with mRNA COVID-19 vaccines are rare. Most patients experiencing these conditions who received care have responded well to treatment and rest and usually can return to their normal daily activities after their symptoms improve. Given the significant potential health risk of COVID-19, including a substantially higher risk of myocarditis than with the COVID-19 vaccine, CDC continues to recommend that individuals ages 12 and older be vaccinated with the relevant FDA-authorized COVID-19 vaccine.

Ad26.COV2.S (Johnson & Johnson/Janssen)

Decades of NIAID support for basic, preclinical, and clinical research on adenovirus (Ad)-based HIV vaccines underpin the development by Johnson & Johnson/Janssen of a coronavirus vaccine candidate based on the Ad26-vector. The vaccine is known as Ad26.COV2.S or JNJ-78436735. NIAID has supported a Phase 3 clinical trial of Ad26.COV2.S through the CoVPN and has provided immunological testing of the candidate using NIAID-funded core laboratory infrastructure. As reported in the *New England Journal of Medicine,* the one-dose vaccine candidate was 66 percent efficacious overall at preventing moderate to severe/critical COVID-19 occurring at least 28 days after vaccination and 85 percent efficacy overall in preventing severe/critical COVID-19 in the Phase 3 trial across several geographical regions, including areas where emerging viral variants predominate. In the United States, the efficacy against moderate to severe/critical disease 28 days after vaccination with Ad26.COV2.S was 72 percent. On February 27, 2021, the FDA issued an EUA for Ad26.COV2.S for prevention of COatients

disease begins to decrease over time following the primary vaccine series; this effect is likely exacerbated by the SARS-CoV-2 Delta variant which is much more transmissible than previous strains of the virus.

On September 22, 2021, and October 20, 2021, FDA amended the EUAs for the Pfizer/BioNTech and Moderna COVID-19 vaccines, respectively, to allow for use of a single booster dose at least 6 months after completion of the primary series in the following groups: individuals 65 years of age and older, and those 18

AZD1222 COVID-19 vaccine candidate uses a chimpanzee adenovirus-vectored vaccine approach developed by researchers at the University of Oxford in collaboration with scientists at NIAID's Rocky Mountain Laboratories. On March 25, 2021, AstraZeneca announced an updated interim analysis of AZD1222 reporting that the vaccine candidate was 100 percent effective at preventing severe COVID-19 disease. Novavax's NVX-CoV2373 COVID-19 vaccine candidate uses a protein nanoparticle vaccine approach. On September 23, 2021, Novavax published data in the *New England Journal of Medicine* showing that NVX-CoV2373 demonstrated 89.7% protection against SARS-CoV-2 infection and

Understanding the Nature of Immunity to SARS-CoV-2

NIAID is conducting and supporting research to enhance our knowledge of immunity against SARS-CoV-2 and to identify components of the immune response that provide protection against COVID-19. NIAID also is examining the quality and durability of the immune response to SARS-CoV-2, generating information that may be leveraged to develop novel SARS-CoV-2 therapeutics or vaccines and inform public health measures.

Data on infection-induced immunity from natural infection with SARS-CoV-2, including studies by NIAID scientists and NIAID-supported researchers, clearly demonstrate that most individuals generate a protective immune response to COVID-19 after infection. However, uncertainty surrounds several variables that can affect the generation of a protective immune response to SARS-CoV-2 following either infection or vaccination. Variables affecting the immune response include

important to note that although we are learning important information about T cell responses in SARS-CoV-2 infected and vaccinated individuals, we still do not know the extent to which T cell responses mediate protection against COVID-19.

NIAID researchers have analyzed the immune responses of individuals who recovered from COVID-19 prior to the emergence of variants and demonstrated that their T cells – a key component of the immune response to SARS-CoV-2—also were capable of recognizing the three most widespread SARS-CoV-2 variants at the time, Alpha (also known as B.1.1.7), Beta (B.1.351), and Gamma (P1). These findings, published in *Open Forum Infectious Diseases,* shed new light on the role of T cells in the development of immune responses to SARS-CoV-2 and suggest that these cells also may help protect against emerging variants of concern.

To help prepare for future pandemic threats, the NIAID VRC has established the Pandemic Response Repository through Microbial/Immune Surveillance and Epidemiology (PREMISE) program. The program will use data from the measurement of T and B cell immune responses to inform the discovery and development of diagnostic, prophylactic, and therapeutic countermeasures and accelerate the global response to pandemic threats. NIAID anticipates the research conducted by PREMISE will advance our knowledge of immune response to vaccination and infection and help inform the response to future pandemic threats.

Identifying Therapeutics to Treat COVID-19

Safe and effective therapeutics are urgently needed to treat patients with COVID-19. NIAID has worked quickly from the earliest days of the pandemic to evaluate promising therapeutics for COVID-19 in rigorous, randomized, controlled clinical trials.

The Adaptive COVID-19 Treatment Trial

NIAID launched a multicenter, randomized placebo-controlled clinical trial, the Adaptive COVID-19 Treatment Trial (ACTT), to evaluate the safety and efficacy of multiple investigational therapeutics for COVID-19. ACTT-1 examined the antiviral drug remdesivir for treatment of severe COVID-19 in hospitalized adults. Based on positive data from ACTT-1, the FDA approved the use of remdesivir for treatment in adults and children 12 years of age and older and weighing at least 40 kg hospitalized due to COVID-19. ACTT-2 evaluated the anti-inflammatory drug baricitinib in combination with remdesivir, and based on favorable data from ACTT-2, the FDA issued an EUA for the use of baricitinib in combination with remdesivir for treatment of adults and

condition. Zyesami is a synthetic version of vasoactive intestinal peptide, which is made naturally in the human body and appears to have lung-protective antiviral and anti-inflammatory effects.

NIH recently launched the Antiviral Program for Pandemics, a collaboration between NIH and BARDA that aims to develop safe and effective antivirals to treat and prevent SARS-CoV-2 infection. The program also will build sustainable platforms for targeted drug discovery and development of antivirals directly targeting viruses with pandemic potential. As part of this effort, NIAID will establish Antiviral Drug Discovery Centers for Pathogens of Pandemic Concern. These multidisciplinary research centers will create platforms that will target coronaviruses and additional RNA viruses with pandemic potential, helping to better prepare the nation for future viral threats. Oral drug candidates for broad use in outpatient settings are the primary focus of this effort.

recommendations to health care providers regarding specific COVID-19 treatments, based on the best available science. The Guidelines address considerations for special populations, inc pregnant women and children. Each Treatment Guidelines section is developed by a working group of Panel members with expertise in the area addressed in the specific section; these members conduct systematic, comprehensive reviews of relevant information and scientific literature. The Panel comprises representatives of NIH and five other federal agencies along with representatives of eleven professional organizations, academic experts, and treating physicians including providers from high COVID-19 incidence areas, and community representatives. The Panel meets regularly to evaluate possible treatment options for COVID-19 and update the Treatment Guidelines as new clinical evidence emerges.

NIAID also is conducting and supporting comprehensive studies to understand the ability of vaccine-induced antibodies to neutralize the variant viruses. On March 25, 2021, NIAID launched

study investigated whether adults in the United States without a confirmed history of SARS-CoV-2 infection have antibodies to the virus, thus indicating prior infection. Findings from the first time point of this longitudinal study suggest that the prevalence of COVID-19 may have exceeded the number of cases medically diagnosed by an additional 16.8 million infections through mid-July 2020. Continued analysis of the 1-year follow-up data from the study will be important in better understanding mortality rates, prevalence of immunity, and the impact SARS-CoV-2 has had on various communities in the United States.

NIAID scientists are participating in leadership of the COVID Human Genetic Effort, an international consortium of hospitals and genetic sequencing hubs that aims to discover genetic factors conferring resistance to SARS-CoV-2 infection or predisposing to severe COVID-19 disease. The consortium has identified a subgroup of patients with severe COVID-19 that have ineffective immune responses to SARS-CoV-2, some of whom have mutations in key immune pathways.

NIAID also supports efforts to understand the rare, but extremely serious, multisystem inflammatory syndrome in children (MIS-C) that has been associated with SARS-CoV-2 infection in children and adolescents. NIAID hosted a virtual workshop on MIS-C with scientists and clinicians from academia, NIH, FDA, and industry, and a report of the workshop recommendations was published on November 2, 2020. NIAID also supports the Pediatric Research Immune Network on SARS-CoV-2 and MIS-C (PRISM) to evaluate acute and long-term clinical and immunological effects of MIS-C and SARS-CoV-2 infection in children. In addition, NIAID is collaborating with Children's National Medical Center to follow 1,000 children with a history of SARS-CoV-2 infection, including those with MIS-C, to determine long-term effects of the illness. NIAID is participating in a trans-NIH effort to coordinate MIS-C research led by NHLBI and the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development. This centralized effort, the Collaboration to Assess Risk and Identify Long-term Outcomes for Children with COVID (CARING for Children with COVID), will permit data to be shared across studies to determine the spectrum of illness and predict long-term consequences of infection.

Monitoring the Long-term Effects of COVID-19

Many people who have had COVID-19 experience continued symptoms or other sequelae as they transition from the acute to post-acute phases of the disease, and we continue to learn more about the duration and manifestations of COVID-19 as we hear from these patients. In December

knowledge to develop safe and effective interventions to diagnose, treat, and prevent SARS-CoV-2